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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/948,149	10/09/1997	BRIAN M. FENDLY	11669.266USU2	6683

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EXAMINER	
SWARTZ, RODNEY P	

ART UNIT	PAPER NUMBER
1645	

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08/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	08/948,149	FENDLY ET AL.	
	Examiner	Art Unit	
	Rodney P. Swartz, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-40,42-45,49-57,59,61 and 62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-40,42-45,49-57,59,61 and 62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' Response to Office Action, received 30 May 2007, is acknowledged. Claims 28, 32, 33, 34, 35, 40, and 42 have been amended. Claims 46-48, 58, 60, and 63-65 have been canceled.

2. Claims 28-40, 42-45, 49-57, 59, 61, and 62 are pending and under consideration.

Rejections Moot

3. The rejection of claim 58 under 35 U.S.C. 103(a) as being unpatentable over Shepard et al (*J. Clin. Immunol.*, 11(3):117-127, 1991), or Lewis et al (*Cancer Immunol. Immunother.*, 37:255-263, 1993), in view of Fendly et al (*Cancer Research*, 50:1550-1558, 1990), Deshane et al (*J. Invest. Med.*, 43(Suppl. 2):328A, 1995), and further in view of Senter et al (U.S. Pat. No. 4,975,278) is moot in light of the cancelation of the claim.

4. The rejection of claims 46-48, and 60 under 35 U.S.C. 103(a) as being unpatentable over Shepard et al (*J. Clin. Immunol.*, 11(3):117-127, 1991) in view of Lewis et al (*Cancer Immunol. Immunother.*, 37:255-263, 1993) and Fendly et al (*Cancer Research*, 50:1550-1558, 1990), and further in view of Deshane et al (*J. Invest. Med.*, 43(Suppl. 2):328A, 1995), and Senter et al (U.S. Pat. No. 4,975,278) is moot in light of the cancelation of the claims.

5. The rejection of claim 63 under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Shepard et al (*J. Clin. Immunol.*, 11(3):117-127, 1991) is moot in light of the cancelation of the claim.

6. The rejection of claim 63 under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lewis et al (*Cancer Immunol. Immunother.*, 37:255-263, 1993) is moot in light of the cancelation of the claim.

7. The rejection of claim 64 under 35 U.S.C. 103(a) as being unpatentable over Shepard et al (*J. Clin. Immunol.*, 11(3):117-127, 1991), or Lewis et al (*Cancer Immunol. Immunother.*, 37:255-263, 1993), in view of Fendly et al (*Cancer Research*, 50:1550-1558, 1990) is moot in light of the cancelation of the claim.

8. The rejection of claim 65 under 35 U.S.C. 103(a) as being unpatentable over Shepard et al (*J. Clin. Immunol.*, 11(3):117-127, 1991), or Lewis et al (*Cancer Immunol. Immunother.*, 37:255-263, 1993), in view of Fendly et al (*Cancer Research*, 50:1550-1558, 1990) is moot in light of the cancelation of the claim.

Rejections Maintained

9. The rejection of claims 28-31, 37, 38, 40, 56, and 57 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Shepard et al (*J. Clin. Immunol.*, 11(3):117-127, 1991) is maintained for reasons of record.

Applicants argue that the cited reference does not disclose antibody binding to the 7C2 epitope and inducing apoptosis. Shepard et al did not determine the properties of antibody 7C2. The data in Table III actually teach away from using antibody 7C2 or an antibody binding to the same epitope to induce apoptosis because the data shows that antibody 7C2 stimulated cell proliferation in breast carcinoma cell line which overexpresses Her2.

The examiner has considered applicants' argument, but does not find it persuasive. Instant claim 28 is drawn to a method comprising only one listed step, i.e., exposing a cell that overexpresses ErbB2 to an effective amount of an isolated antibody that binds to epitope 7C2/7F3 of ErbB2. As stated in the prior rejection explanations, Shepard et al do teach exposing a cell that overexpresses ErbB2 (also known as HER2) to an effective amount of an isolated antibody (monoclonal antibody 7C2 and monoclonal antibody 7F3) that binds to epitope

7C2/7F3 of ErbB2. These monoclonal antibodies in the reference designated as 7C2 and 7F3 are the same antibodies of the instant application which are also listed as 7C2 and 7F3. Contrary to applicants' argument that antibody 7C2 stimulated cell proliferation in breast carcinoma cell line which overexpresses Her2, the data show that the binding of either antibody resulted in inhibition of proliferation of the cell by 21% and 38% respectively when compared to cell growth in the absence of the antibodies. Thus, while Shepard et al may not label their methodology as "apoptosis", they do teach the only methods steps recited by the instant claims, i.e., binding a cell that overexpresses ErbB2 to an effective amount of an isolated antibody that binds to epitope 7C2/7F3 of ErbB2.

10. The rejection of claims 28-31, 37, 38, and 40 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lewis et al (*Cancer Immunol. Immunother.*, 37:255-263, 1993) is maintained for reasons of record.

Applicants argue that Lewis et al do not disclose antibody induction of apoptosis.

The examiner has considered applicants' argument, but does not find it persuasive. Instant claim 28 is drawn to a method comprising only one listed step, i.e., exposing a cell that overexpresses ErbB2 to an effective amount of an isolated antibody that binds to epitope 7C2/7F3 of ErbB2. As stated in the prior rejection explanations, Lewis et al do teach exposing a cell that overexpresses ErbB2 (also known as HER2) to an effective amount of an isolated antibody (monoclonal antibody 7C2 and monoclonal antibody 7F3) that binds to epitope 7C2/7F3 of ErbB2. These monoclonal antibodies in the reference designated as 7C2 and 7F3 are the same antibodies of the instant application which are also listed as 7C2 and 7F3. The data show that the binding of either antibody resulted in inhibition of proliferation of the HER2 (ErbB2) cell by 79% and 30% respectively when compared to cell growth in the absence of the

antibodies (Table 2). Thus, while Lewis et al may not label their methodology as "apoptosis", they do teach the only methods steps recited by the instant claims, i.e., binding a cell that overexpresses ErbB2 to an effective amount of an isolated antibody that binds to epitope 7C2/7F3 of ErbB2.

11. The rejection of claims 32-36, and 39 under 35 U.S.C. 103(a) as being unpatentable over Shepard et al (*J. Clin. Immunol.*, 11(3):117-127, 1991), or Lewis et al (*Cancer Immunol. Immunother.*, 37:255-263, 1993), in view of Fendly et al (*Cancer Research*, 50:1550-1558, 1990), Deshane et al (*J. Invest. Med.*, 43(Suppl. 2):328A, 1995), and further in view of Senter et al (U.S. Pat. No. 4,975,278) is maintained for reasons of record.

Applicants' arguments and examiner's response to argument concerning Shepard et al and Lewis et al are discussed, *supra*.

Applicants argue that Fendly et al, Deshane et al, and Senter et al do not characterize the antibody or disclose antibody binding to an epitope for inducing apoptosis.

The examiner has considered applicants' argument, but does not find it persuasive. Shepard et al and Lewis et al do disclose monoclonal antibodies designated as 7C2 and 7F3 which are the same antibodies of the instant application, also listed as 7C2 and 7F3. Fendly et al is cited as a reference for production and further characterization of the monoclonal antibodies designated as 7C2 and 7F3. Deshane et al is cited as a reference for teaching that intracellular antibody knockout of the ErbB2 oncoprotein results in induction of apoptosis of tumor cell targets. Senter et al is cited as a reference for teaching a method for delivery of cytotoxic drugs to tumor cells by using a tumor specific antibody/enzyme conjugate that binds to tumor cells. Thus, the references of Fendly et al, Deshane et al, and Senter et al were

utilized for disclosing aspects of the claims not specifically delineated in either Shepard et al or Lewis et al.

12. The rejection of claims 42-45, 49-55, 59, 61, and 62 under 35 U.S.C. 103(a) as being unpatentable over Shepard et al (*J. Clin. Immunol.*, 11(3):117-127, 1991) in view of Lewis et al (*Cancer Immunol. Immunother.*, 37:255-263, 1993) and Fendly et al (*Cancer Research*, 50:1550-1558, 1990), and further in view of Deshane et al (*J. Invest. Med.*, 43(Suppl. 2):328A, 1995), and Senter et al (U.S. Pat. No. 4,975,278) is maintained for reasons of record.

Applicants' arguments and examiner's response to argument concerning Shepard et al and Lewis et al are discussed, *supra*.

Applicants argue that Fendly et al, Deshane et al, and Senter et al do not characterize the antibody or disclose antibody binding to an epitope for inducing apoptosis.

The examiner has considered applicants' argument, but does not find it persuasive. Shepard et al and Lewis et al do disclose monoclonal antibodies designated as 7C2 and 7F3 which are the same antibodies of the instant application, also listed as 7C2 and 7F3. Fendly et al is cited as a reference for production and further characterization of the monoclonal antibodies designated as 7C2 and 7F3. Deshane et al is cited as a reference for teaching that intracellular antibody knockout of the ErbB2 oncoprotein results in induction of apoptosis of tumor cell targets. Senter et al is cited as a reference for teaching a method for delivery of cytotoxic drugs to tumor cells by using a tumor specific antibody/enzyme conjugate that binds to tumor cells. Thus, the references of Fendly et al, Deshane et al, and Senter et al were utilized for disclosing aspects of the claims not specifically delineated in either Shepard et al or Lewis et al.

Rejection Necessitated by Amendment

Claim Rejections - 35 USC § 112

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 42-45, 59, 61, and 62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Newly amended claim 42 now depends from newly amended claim 28.

Newly amended claim 28 is drawn to a method for inducing apoptosis comprising exposing a cell to an effective amount of an isolated first antibody that binds to epitope 7C2/7F3 of ErbB2.

Newly amended claim 42 recites: The method of claim 28, "further comprising" said antibody and a pharmaceutically acceptable carrier... It is unclear what is meant by this language. For instance, does it mean that "in addition to" the antibody already exposed to said cell that more of the antibody is added or that the antibody of claim 28 was actually already combined with a pharmaceutically acceptable carrier. In addition, claim 42 also recites "wherein the antibody composition" results in a certain activity. It is unclear which antibody is being referred by this new recitation, i.e., the antibody of claim 28, or the "further comprising antibody/carrier" construct.

Claims 43-45, 59, 61, and 62 depend from claim 42, but do not clarify the issue.

Conclusion

15. Claims 28-40, 42-45, 49-57, 59, 61, and 62 are finally rejected.

16. Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rodney P. Swartz, Ph.D., Art Unit 1645, whose telephone number is (571) 272-0865. The examiner can normally be reached on Monday through Thursday from 9:00 AM to 7:30 PM EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Jeffrey Siew, can be reached on (571)272-0787.

The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RODNEY P SWARTZ, PH.D
PRIMARY EXAMINER
Art Unit 1645

August 19, 2007